

Amendments to the Specifications:

Please replace the paragraph starting at page 7, line 23 of the specification with the following paragraph:

The present invention especially relates to detection of nitrated collagen type II protein, wherein the nitrated amino acid is the tyrosine of one of the sequences His-Arg-Gly-Tyr-Pro-Gly-Leu-Asp-Gly (SEQ ID NO: 1) or Leu-Gln-Tyr-Met-Arg-Ala (SEQ ID NO: 2). Synthetic nitrated peptides including these sequences may be used to raise polyclonal and/or monoclonal antibodies, as well as cell lines producing such monoclonal antibodies.

Please replace the paragraph starting at page 12, line 24 of the specification with the following paragraph:

A preferred marker protein is collagen type II. Collagen type II contains two tyrosine's, which can be nitrated upon oxidative damage. The first sequence HRGYPGLDG (His-Arg-Gly-Tyr-Pro-Gly-Leu-Asp-Gly) (SEQ ID NO: 1) is localised in the triple helical region while the second sequence LQYMRA (Leu-Gln-Tyr-Met-Arg-Ala) (SEQ ID NO: 2) is located in the non-helical domain at the C-telopeptide. The amino acids sequences including the tyrosine residues are specific for type II collagen and can be employed as specific biochemical markers of catabolic processes in the cartilage tissue.

Please replace the paragraph starting at page 15, line 14 of the specification with the following paragraph:

In situations where a tissue sample is used for monitoring of pathological processes in joint tissue, there is a strong likelihood that denatured helical collagen domains, resulting from catabolic processes within the tissue, might be retained in the tissue by cross-linking and fibrillar packaging.

To address this problem, the biological sample is first contacted with an enzyme having the ability to selectively cleave unwound (non-helical) collagens without cleaving the His-Arg-Gly-Tyr-Pro-Gly-Leu-Asp-Gly (SEQ ID NO: 1) and/or the Leu-Gln-Tyr-Met-Arg-Ala (SEQ ID NO: 2) epitope. Such enzymes could be, but is not limited to, trypsin or chymotrypsin, which are unable to cleave wound (native) collagen within the α -helix. The fragments of unwound collagen are then extracted from the biological sample to produce an extract of unwound collagen fragments. This extract can then be assayed as mentioned in the above.

Please replace the paragraph starting at page 19, line 4 of the specification with the following paragraph:

FIG. 2 shows competitive inhibition of antiserum D37 binding to His-Arg-Gly-Tyr:NO₂-Pro-Gly-Leu-Asp-Gly coated plates using His-Arg-Gly-Tyr:NO₂-Pro-Gly-Leu-Asp-Gly (SEQ ID NO: 1) (O), His-Arg-Gly-Tyr-Pro-Gly-Leu-Asp-Gly (SEQ ID NO: 1) (●), native type II collagen (◆), nitrated type II collagen (◇), type I collagen (), BSA () and nitrated BSA (∇) as competitors. B/Bo represents the ratio between antibody bound to coated antigen in the presence of competitor antigen (B) or in the absence of competitor antigen (Bo) and is given in percentage;

Please replace the paragraph starting at page 21, line 8 of the specification with the following paragraph:

Six antisera, identified as Coll2-1:NO2 D35, D36, D37, D38 D39 and D40, were obtained and their specificity were tested with the competitive inhibitions His-Arg-Gly-Tyr(NO₂)-Pro-Gly-Leu-Asp-Gly, His-Arg-Gly-Tyr-Pro-Gly-Leu-Asp-Gly (SEQ ID NO: 1), type II nitrated collagen, native type II collagen, type I nitrated collagen I, type I collagen, nitrated BSA and BSA.

Please replace the paragraph starting at page 22, line 22 of the specification with the following paragraph:

The antisera produced, were tested for their specificity for His-Arg-Gly-Tyr:NO2-Pro-Gly-Leu-Asp-Gly, by use of the immunoassay described in example 1. To test for specificity His-Arg-Gly-Tyr:NO2-Pro-Gly-Leu-Asp-Gly, His-Arg-Gly-Tyr-Pro-Gly-Leu-Asp-Gly (SEQ ID NO: 1) peptide, type II nitrated collagen, native type II collagen, type I nitrated collagen, type I collagen, nitrated BSA and BSA.

Please replace the paragraph starting at page 22, line 29 of the specification with the following paragraph:

Native type II collagen, type I collagen, nitrated collagen type I, nitrated BSA and BSA, were not able to compete with the coated His-Arg-Gly-Tyr:NO2-Pro-Gly-Leu-Asp-Gly peptide in the applied concentrations, whereas the antiserum showed weak affinity to the non-Nitrated His-Arg-Gly-Tyr-Pro-Gly-Leu-Asp-Gly sequence (SEQ ID NO: 1) and nitrated collagen type II and strong affinity to the His-Arg-Gly-Tyr:NO2-Pro-Gly-Leu-Asp-Gly sequence. A lack of binding affinity has also been demonstrated with L-nitrotyrosine.